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Lower Respiratory Infections among Children: Are Viruses a Serious Threat?

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Abstract: Acute lower respiratory tract infections (ALRIs) are the main cause of morbidity and mortality in younger children. It accounts for one fifth of all deaths in children below 5 years of age. In India not many studies are available about viral etiology of LRTI, so this study was done to determine viral etiologies of lower respiratory tract infections among children from one month to five years of age and to determine clinical profile of patients presenting with lower respiratory tract infections. Hospital based descriptive type of observational study conducted at SMS Medical College, Jaipur. 130 cases of lower respiratory tract infections who were hospitalized with the symptoms of cough, fever, and rapid breathing were studied. Cases were categorized into two groups: less than one year and more than one year. Their history, clinical examination and lab investigations were recorded on a proforma. Nasopharyngeal aspirates and nasopharyngeal swabs were tested for a panel of 8 viruses ie. RSV, Adeno, PIV-1, PIV-2, PIV-3, hMPV, Influenza A (FLUAV) and Influenza B (FLUBV) by RT PCR. Out of 130 cases, viruses were isolated from 90(69.23%), 83(63.8%) samples showed a single virus and 7(5.38%) samples showed multiple viruses. Most common viral organism in both age groups was RSV (83.3 % in < 1 year and 53 % in > 1 year) but the prevalence of other viruses like influenza B and Adenovirus was more in >1 year (23%,15.3% respectively) than in < 1 year of age (5.9% in both). Clinically cough, fever and rapid breathing was observed in all the cases while 114 (87.69%) cases had chest retractions and 86 (66.15%) cases had coryza. In the present study, viruses were the most common etiology of LRTIs in hospitalized children less than five year old . RSV was the most common organism in both age groups but the prevalence of other viruses like Adenovirus and influenza B increased in older age group. RSV predominantly presented as bronchiolitis while Influenza predominantly presented as pneumonia. As viruses were isolated from 90(69.23%) samples so antibiotics should be used judiciously in these children where co infection or secondary bacterial infections are a serious consideration.. Viral etiology of LRTI was consistant with clinical finding of cough & coryza where as presence of toxaemia& dehydration are consistant with nonviral etiology.
Keywords: lower respiratory tract infections, respiratory viruses, RT PCR.

INTRODUCTION

Acute respiratory infections (ARIs) are among the leading cause of morbidity and mortality in children under five years in developing countries UNICEF reported that in 2015, ARI is responsible for 15% of under 5 death causing 9,20,136 deaths globally and 1,78,994 deaths in India. In India, ARI accounts for 30-50% of visits to health facilities and 20-40% of hospital admissions. Under five death rates from ARI per1000 live birth is 7 both in India and globally. Most of the victims were less than 2 years old [1].

ARI is defined as a new episode occurring in an individual who has been free of symptoms for at least 48 hours and lasting for less than 30 days duration except those of the middle ear where the duration of acute episode is less than 14 days [2].

Acute respiratory infection is an infection of any part of respiratory tract or any related structures including paranasal sinuses, middle ear and pleural cavity. Respiratory tract infections are categorized into two i.e., lower respiratory tract infections (LRTIs) and upper respiratory tract infections (URTIs) according to the site of infection. URTI include rhinitis (common cold), sinusitis, ear infections (Otitis Media), acute

pharyngitis or tonsillopharyngitis, epiglotitis and laryngitis. LRTI in children includes pneumonia, bronchiolitis, tracheitis and bronchitis [3].

The causative agents of ARI include bacterial (e.g. *Streptococcus pneumoniae*, *Haemophilus influenzae, Staphylococcus aureus,etc.*), viral (such as influenza, metapneumovirus, parainfluenza, respiratory syncytial virus, and adenovirus) and atypical organism (Chlamydia and mycoplasma) are important organism in grownup children. However viruses are important causes of upper and lower respiratory tract diseases in infants and young children [3, 4]

Due to the lack of sensitivity and specificity of symptoms of LRTI, it is difficult to differentiate between bacterial and viral etiology. Early diagnosis of etiology facilitates institution of early specific antimicrobials which is essential to decrease LRTI related morbidity and mortality[3]**.** In routine practice many times irrational empirical antibiotics are commonly used in the management of pneumonia. But antibiotic use was not found to be much effective in randomised trials as bacterial etiology was not found in majority of the cases. In this context, diagnosis of viral etiology can prevent irrational use of antibiotics [5].

Plenty of data are available for developed countries which highlighs the facts that majority of LRTI in young children are due to different viruses. There is scarcity of data from developing countries including India to support this fact. Hence present study was planned to analyze this situation in our scenario.

METHODS

This study was a descriptive type of observational study conducted over a period of one year at the Department of Pediatric Medicine, SMS Medical College, Jaipur. Institutional ethical committee approval was taken prior to the study. 130 hospitalized subjects admitted with diagnosis of severe LRTIs were taken for the study purpose. Once the inclusion was made after getting informed consent from the parents, baseline data including age, sex, immunization status, family history of tuberculosis, atopy, diet history, vitals, clinical examination, laboratory investigations and radiological findings were recorded for each case. Cases were categorized into two groups: less than one year and more than one year. Nasopharyngeal aspirates and nasopharyngeal swabs were collected with all aseptic precautions and transported to laboratory in viral transport media (VTM) tube and tested for a panel of 8 viruses: RSV, Adeno, PIV-1, PIV-2, PIV-3, hMPV, Influenza A (FLUAV) and Influenza B (FLUBV) by RT PCR by Automated Easymag Biomerurix machine.

AIMS AND OBJECTIVES

- To determine viral etiologies (panel of eight viruses) of lower respiratory tract infections among children from one month to five years of age.
- To determine clinical profile of patients presenting with lower respiratory tract infections.

Inclusion criteria

A) Hospitalised Children of age group one month to five years, presenting with following symptoms:
   Cough, fever, rapid breathing (as per WHO Criteria) [6, 7]

B) Children whose parents gave positive consent.

*RR was counted for one minute after nasal clearing and when the child was afebrile.

Based on the following clinical and radiological criteria acute LRTI was classified into Bronchiolitis and Pneumonia.

Bronchiolitis is characterized by low-grade fever, coryza, progressing to cough, tachypnea, chest indrawing, wheezes, hyperinflated lung field on chest x-ray were diagnosed as Bronchiolitis [8]**.**

Pneumonia is characterized by moderate to high fever, breathing difficulty, crackles, and infiltrates on lung fields on chest X-ray were diagnosed as pneumonia [9].

Exclusion criteria

- Children having congenital respiratory tract malformations.
- Children having bronchopulmonary dysplasia.
- Children having history of choking / suspected foreign body inhalation.
- Children having cardiac diseases.

RESULTS

130 hospitalized cases of lower respiratory tract infections included in the study after applying inclusion and exclusion criteria. Out of 130 study subjects, 104(80%) belonged to age group less than one year. The mean age of the patient in the study group was 7.14 months

Out of the 130 children with LRTIs, viruses were isolated from 90 (69%) samples out of which, 83(63.6%) samples showed a single virus and 7(5.4%) samples showed co-infections (figure1). RSV was the most predominant viral agent found in 71(54.6%) cases followed by influenza-B and Adenovirus found in 6(4.61%) and 3(2.31%) cases respectively. Most common viral organism in both age groups was RSV (83.3 % in < 1 year and 53 % in > 1 year) but the prevalence of other viruses like influenzalu B and Adenovirus was more in >1 year (23%,15.3% respectively) than in < 1 year of age (5.9% in both). RSV presented as bronchiolitis in 74.6% cases. (p= 0.005). Influenza virus presented as Pneumonia in

85.7% cases. (p= 0.019). Clinically cough, fever, and rapid breathing was observed in all the cases, while 114 (87.69%) cases had chest retractions and 86 (66.15%) cases had coryza.

In present study out of 130 cases, RSV was detected in 71(54%) of cases, followed by Influenza B in 6(4.6%) cases (Table-2).

Table-1: Demographic and Clinical Characteristics of the Study Patients (n=130)

PARAMETER	VALUE
Mean age	7.14 months
< 1 Year	104 (80%)
1- 5 Year	26 (20%)
Male	50 (70%)
Female	20(30%)
Provisional diagnosis	
Bronchiolitis	82(63.1%)
Pneumonia	48(36.9%)
Clinical feature	
Fever	130(100%)
Cough	130(100%)
Rapid breathing	130(100%)
Chest retraction	114(87.7%)
Coryza	86(66%)
Refusal to feed	76(58%)
Cyanosis	16(12%)
Dehydration	15(11.5%)
Toxic look	10(7.7%)

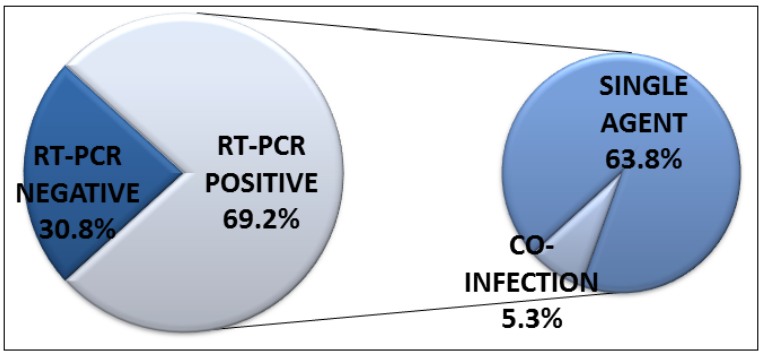

Fig-1: Distribution of the cases according to viral etiology

Table-2: Etiological distribution of LRTI cases

Viruses	RT PCR Positive No (%)
RSV	71(54.62)
Influenza-B	6(4.62)
Adeno & RSV	4(3.08)
Adeno	3(2.31)
Influenza-A	1(0.77)
Influenza-B & hMPV	1(0.77)
Influenza-B & RSV	1(0.77)
Parainfluenza 3	1(0.77)
Perainfluenza 1	1(0.77)
RSV & para influ 3	1(0.77)
Negative	40(30.77)
Total	130(100.00)

Table-3: Distribution of viral agents according to age group

Agents	<1 year (84 cases) N (%)	>1 year (13 cases) N (%)
Rsv	70(83.3)	7(53)
Adeno	5(5.9)	2(15.3)
Influenza b	5(5.9)	3(23)
Parainfluenza 3	2(2.3)	0(0)
Influenza a	1(1.1)	0(0)
Hmpv	1(1.1)	0(0)
Parainfluenza 1	0(0)	1(7.6)
Parainfluenza 2	0(0)	0(0)

In our study the most common viral organism in both age groups was RSV(83.3 % in age group < 1 year and 53 % in age group > 1 year) but the prevalence of other viruses like Flu B and Adenovirus was more in >1 year (23%,15.3% respectively) than in < 1 year age (5.9% both).

Table-4: Association of Influenza virus with Pneumonia and Bronchiolitis

Agent	Pneumonia	Bronchiolitis	P-value
RSV (N=71)	18 (25.3%)	53 (74.6 %)	0.005
Infiuenza	6(85.7%)	1(14.3%)	0.019

In our study out of 71 cases of RSV, 53(74.6%) cases presented as bronchiolitis and 18(25.3%) cases presented as pneumonia and out of 7 cases of Influenza, 6(85.7%) cases presents as pneumonia and 1(14.3%) case presented as bronchiolitis.

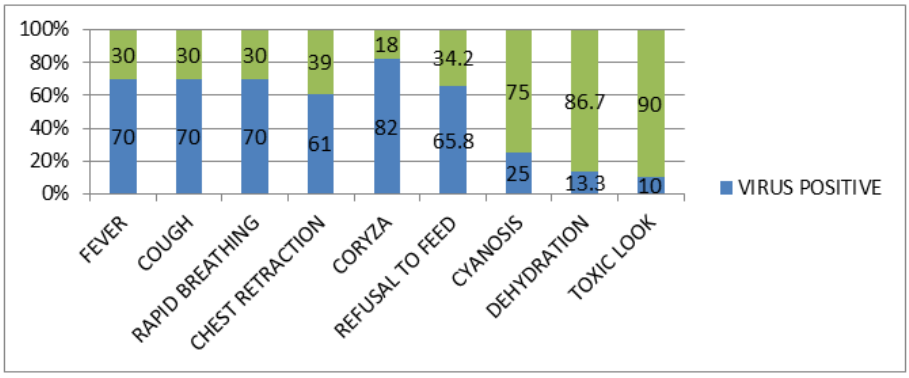

Fig-2: Shows that among clinical features, coryza was most consistantly associated with viral etiology while toxic look was commonly associated with nonviral etiology.

DISCUSSION

We conducted an observational study in tertiary care teaching institute (SPMCHI) over a period of 1 year (from Sept. 2015 to June 2016). In our study we included 130 hospitalized cases of LRTI. Out of 130 cases, male & female participants were 70% & 30% respectively and the male;female ratio was 2.3:1.

Our study included patients between 1 to 60 months of age and the mean age of subjects was 7.14 months. We divided study population into two age groups (i) less than one year and (ii) more than one year. Out of 130 cases 104(80%) were less than one year and 26(20%) cases were more than one year of age.

In our study out of 130 cases of lower respiratory tract infections, 90 (69.23%) were tested positive for viruses. Out of these 90 cases, 83(63.84%) showed infection with one viral agent and rest 7 (5.38%) had coinfection with two viral agents. Remaining 40 cases of lower respiratory tract infections probably had non viral etiology or viral etiology which was not included in our viral profile.

Caroline F Shafik *et al.*, [10] studied 450 children out of which virus was positive in 269(59.9%) cases. In the study by Eun Hwa Choi *et al.*, [11] 515 subjects under five years age were included and they reported that 312(60.6%) cases were positive for viruses. Akira Suzuki *et al.*, [12] study included 819 patients under thirteen year of age and virus was detected in 501 (61.2%) cases. All above study results

are in concordance with our study. While a lower incidence was found in the study by MS Chhaddha *et al*., [13] where they included 188 subjects of lower respiratory tract infections under fourteen years of age and showed viral etiologies in 45.7% cases. This discrepancy may be due to difference in age group of the study population.

In our study out of 130 subjects, RSV was the most predominant virus found in 71(54.61%) cases. Emerson Rodrigues da Silva *et al*., [14] study included 260 children under three years of age and showed RSV in 54% cases. In Caroline F Shafik *et al*., [10] study out of 450 subjects under five year age, Respiratory Syncytial Virus (RSV) was the most predominant found in 23.8%. MS Chhaddha *et al*., [13] was included 188 subjects with lower respiratory tract infections under 14 years of age and RSV was detected in 21.3% cases. In these studies, the predominant agent was RSV which was similar to our study. In contrast, Yanqin Lu *et al*., [15] study included 323 children up to 13 years of age and demonstrated Parainfluenza virus in 27% cases, RSV in 9.91% and Influenza virus in 5.57% cases. Our results are not in concordance with this study probably due to different age group of study population suggesting that the incidence of RSV decreased with increasing age.

In our study we divided subjects in two age groups i.e. less than one year and more than one year. Most common viral organism in both age groups was RSV but the prevalence of other viruses like Flu B and Adenovirus was more in >1 year age group (23%, 15.3% respectively) than in < 1 year (5.9% in both).

In Caroline F Shafik *et al*., [10] 450 subjects two groups of less than one year (61.5%) and more than one year(42.5%) Among less than one year age group, RSV (29.71%) was the most common etiological agent, followed by Adenovirus (14.13%) and Influenza B virus (0.36%) but in more than one year age group, Adenovirus (25.58%) was the most common etiological agent followed by RSV (14.5%) and Influenza B virus (2.32%). In the study by MS Chhaddha *et al*. [13] 188 NPAs were screened for respiratory viruses, of which 45.7% tested positive. RSV was most commonly detected with 21.3% positivity followed by measles virus (8.5%), Influenza A virus (7.4%), ADV (5.3%), Influenza B virus (1.6%) and hMPV (1.1%). Positivity rate of RSV was highest in children aged < 1 year, which decreased with increase in age, while positivity rate of Influenza virus increased with increasing age. Eun Hwa Choi *et al*., [11] studied the age distributions of infants and children associated with each virus. LRTIs caused by RSV were predominant among younger infants (mean age, 9 months), compared with LRTIs associated with adenovirus, HBoV, hMPV, or influenza A (P = .01 for each comparison). In particular, a greater proportion of RSV infections occurred in infants $\leq$ 3 months old, compared with other virus-associated LRTIs (P = .04 for all comparisons between RSV and 6 viruses [adenovirus, HBoV, PIV-3, influenza virus A, hMPV, and HCoV-NL63]) In contrast, adenovirus, hMPV, and Influenza virus were more frequently detected in children >24 months old. These studies indicated that the incidence of RSV was higher in younger age group while in older children other viruses like Adenovirus and Influenza virus were more predominant.

In total 130 cases, RSV was detected in 71(54.6%) cases among these 53(74.6%) presented as Bronchiolitis and 18(25.3%) presented as Pneumonia.

Solange Oue´draogo *et al.*, [16] study RSV detected in 19 cases. Among these 19 cases, 10 (52.6%) presented as Bronchiolitis and 6 (31.6%) presented as Pneumonia. Their results are in concordance with our results.

In total 130 cases, Influenza virus was detected in 7 cases among these 6(85.7%) presented as Pneumonia and 1(14.3%) presented as Bronchiolitis. In the study by Eun Hwa Choi *et al*., [11] Influenza virus was associated with 12(54.6%) cases presented as Pneumonia and 3(13.6%) cases of Bronchiolitis. The results this study are in concordance with our study.

In our study, regarding the clinical manifestations- cough, fever, and rapid breathing was observed in all the cases, while 114 (87.69%) cases had chest retractions and coryza was seen in 86 (66.15%) cases. In Caroline F Shafik *et al*., [10] study of LRTI in 450 patients, the most common clinical feature was cough (98%) followed by difficulty in breathing (93%) ,chest indrawing (76%) and fever(73%). Akira Suzuki *et al*., [12] study showed clinical manifestation on admission were cough present in 99.9% cases, chest indrawing in 98.7% cases, difficulty of breathing 81.9% cases, cyanosis in 7.6% cases.

CONCLUSION

In the present study, viruses were the most common etiology of LRTIs in less than five year old children. RSV was the most common organism in both age groups but the prevalence of other viruses like Adenovirus and influenza B increased in older age group. RSV predominantly presented as bronchiolitis while Influenza predominantly presented as pneumonia. The presence of nasal symptoms and absence of toxemia can be a clinical clue to the viral etiology of LRTI in situations where virus isolation is not practical and feasible.

RECOMMENDATIONS

In the light of above observations, we recommend that majority of LRTIs in younger children are caused by different respiratory viruses. Hence, routine use of antibiotics is irrational in most of the situations. So use of Antibiotics should be restricted to

conditions where either coinfection or secondary infection with bacteria is in strong consideration.

LIMITATIONS

The major limitation of our study is that viral panel used for detection of viruses by RT-PCR included only 8 viruses. Hence we had more false negative cases. In our study the sample was not taken from the lower respiratory tract by BAL, which is considered the gold standard. We had taken samples of nasopharynx which may not be true representative of causative agent. Hence the causal relationship may be erroneous. Another limitation was smaller size of our study population.

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